

## **REMARKS**

### **ADMINISTRATIVE ISSUES**

#### Drawings

The drawings filed with the application on January 3, 2002 have not been accepted as formal or denied by the examiner. Applicants request that the examiner accept or deny the filed drawings in the next communication.

#### Information Disclosure Statement

The Information Disclosure Statement (IDS) filed on September 17, 2002 was formerly considered by the examiner. However, references AB-1 and AC-1 have not been acknowledged or initialed by the examiner. Applicants request that the examiner acknowledge and initial all references cited in the September 17, 2002 IDS in the next communication.

#### Priority

The benefit of applicants' priority document, U.S. provisional application 60/259,818 filed January 4, 2001, has not been formally acknowledged by the examiner. The cross-reference to this provisional application was made on the first page of the application as filed. Further, a claim for priority under 35 U.S.C. § 119/363 was made in the declaration. Applicants request that the priority claim be formally acknowledged by the examiner in the next communication.

### **STATUS OF THE CLAIMS**

Claims 33-90 are pending. Claims 33, 34, 35, 36, 38, 49, 50, 52, and 90 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Allan *et al.* (U.S. Patent No. 5,747,309;) ("Allan") in view of Dean-Nystrom *et al.* (*Infection and Immunity* 66: 4560-4563, 1998) (Dean-Nystrom"). Claims 37, 39-48, 51 and 53-59 were objected to as being dependent from rejected base claims 33 and 34.

**REJECTIONS UNDER 35 U.S.C. § 103(A)**

The examiner stated that the claims are drawn to a method of reducing colonization/shedding of enterohemorrhagic *E. coli* (EHEC) in a non-human mammal comprising administering a composition comprising an *E. coli* cell culture supernatant.

Allan *et al.* is cited for its alleged teaching of a method for preventing *E. coli* infection (i.e., reducing colonization/shedding of *E. coli*) in a non-human mammal comprising administering a composition comprising an *E. coli* cell culture supernatant (see abstract, claims, and specifically claims 20 and 48, columns 3, 6, 8, 9, and 10). Allen *et al.* is alleged to teach domestic animals such as bovine and ovine (see column 6, lines 38-46. Allen *et al.* is alleged to teach culture supernatant (see column 10, lines 40-45), multiple strains of *E. coli* (see column 12). The examiner points out that Allen *et al.* do not teach *E. coli* O157:H7. However, the examiner is of the opinion that Dean-Nystrom *et al.* teach *E. coli* O157:H7 and intimin vaccines for reduction of EHEC in cattle (directing applicants to read the abstract).

The examiner further alleges that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the methods of Allen *et al.* and Dean-Nystrom *et al.* to obtain the claimed invention. More specifically, the examiner stated that one of ordinary skill in the art would have been motivated to use the specific strains of *E. coli* taught by Dean-Nystrom *et al.*, with the expectation of obtaining a composition containing EHEC to reduce colonization of EHEC in cattle. Applicants respectfully traverse.

Claims cannot be found obvious unless the prior art itself suggests the desirability of the combination. *Berghauser v. Dann*, 204 U.S.P.Q. 393 (D.D.C. 1979); *ACS Hospital Systems Inc., v. Montefiore Hospital*, 221 U.S.P.Q. 929 (Fed. Cir. 1984). There must be something in the prior art that would have motivated persons of ordinary skill to make the combination. *In re Stencel*, 4 U.S.P.Q.2d 1071 (Fed. Cir. 1987), *accord*, *Ex parte Marinaccio*, 10 U.S.P.Q.2d 1716 (Pat. Off. Bd. App. 1989)(combining references is improper absent some teaching, suggestion, or motivation for the combination in the prior art).

Obviousness cannot be established by merely showing that it would have been possible for a person of ordinary skill to combine or modify teachings of the prior art. The prior art must suggest the desirability of the claimed invention. MPEP 2143.01. Moreover, there must be affirmative evidence that such a person would have been “**impelled**” to make

the combination. *Ex parte Levengood*, 28 U.S.P.Q.3d 1300, 1302 (Pat. Off. Bd. App. 1993)(citations omitted). As is stated in M.P.E.P. § 2143, three criteria must be met to establish prima facie obviousness:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Moreover, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention when there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one ordinary skill in the art. MPEP § 2143.01

Here, a *prima facie* case of obviousness has not been established, at least because there is no suggestion or motivation to modify the references and the prior art references when combined, do not teach or suggest all the claim limitations. As will be made clear below, the cited references do not teach the claimed invention and even if combined, one of skill would not be able to arrive at the subject matter as claimed in the claims or disclosed in the instant specification.

In making the assessment of differences between the prior art and the claimed subject matter, section 103 specifically requires consideration of the claimed invention "as a whole." *Ruiz v. A.B. Chance Co.*, 357 F.3d 1270, 1275 (Fed. Cir. 2004). Inventions typically are new combinations of existing principles or features. *Envtl. Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698 (Fed. Cir. 1983) (noting that "virtually all [inventions] are combinations of old elements"). This "as a whole" assessment of the invention requires a showing that an artisan of ordinary skill in the art at the time of invention, confronted by the same problems as the inventor and with no knowledge of the claimed invention, would have selected the various elements from the prior art and combined them in the claimed manner. *Id.* In other words, section 103 requires some suggestion or motivation, before the invention itself, to make the

new combination. *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 2005 U.S. App. LEXIS 10672 at \*11-12 (Fed. Cir. Jun. 9, 2005) (citing *In re Rouffet*, 149 F.3d 1350, 1355-56 (Fed. Cir. 1998)).

In the present analysis, the claimed invention has been broken into its component parts, and a prior art reference corresponding to each component has been cited. This line of reasoning imports hindsight into the obviousness determination by using the invention as a roadmap to find its prior art components and discounts the value of combining various existing features or principles in a new way to achieve a new result - the essence of invention. *Id.* Indeed, one skilled in the art would not have combined Allan *et al.* with Dean-Nystrom *et al.* in an attempt to arrive at the present invention. Allan *et al.* describe the problem to be solved as a need for an effective, easily administered vaccine against infections from pathogenic bacteria, including *E. coli*. (col. 3, lines 60-62). Allan *et al.* summarize their invention as vaccines provided for vaccinating an animal against pathogenic bacteria, including *E. coli* as well as methods of preparing and methods of use of vaccine strains and compositions that result from or are used in these methods. (col. 3, line 65 through col. 4, line 2). Allan *et al.* goes on to summarize various vaccine strains of pathogenic bacteria comprising mutations (pyrimidine pathway mutation, an iron metabolism mutation, and a colicin transport mutation) as another aspect(s) of their invention. (col. 4, lines 3-8). Allan *et al.*'s teaching of culture supernatant (col. 6, lines 38-46) is a procedure for growing cultures of *E. coli* to develop mutant strains.

Allan *et al.* discloses use of live attenuated organisms as vaccines for livestock and poultry. In particular, Allan *et al.* discloses live attenuated organisms with *carAB* and/or *fur* mutations. It is related to *E. coli* which causes disease, in this case respiratory and systemic infections. The reference to supernatants (column 10, lines 40-45) actually refers only to a method for phage P1 transduction which was used to create the mutations, and not to vaccination with supernatant proteins. Thus, it is clearly irrelevant to O157 vaccines. Furthermore, claims 20 and 48 are directed to the prevention of disease (Colisepticemia), not colonization or shedding, and rely on live bacteria as the immunogen (not secreted proteins from EHEC cultures).

Allan *et al.* does not teach or suggest a method of reducing colonization or shedding in a non-human mammal by administering a composition comprising an EHEC cell culture

supernatant, as is presently claimed. In fact, central to the present invention is the discovery that cell culture supernatants derived from EHEC cultures which contain EHEC secreted antigens, produce an immune response in animals to which they are administered and thereby provide protection against EHEC infection, such as protection against colonization. (see Specification, at page 13, lines 22-26.).

The examiner cites Dean-Nystrom *et al.* for the premise of allegedly teaching *E. coli* O157:H7 and intimin vaccines for reduction of EHEC in cattle. Intimin is an outer membrane protein on various *E. coli*. Intimin is *not* a secreted protein (but an integral membrane protein). This differs significantly from the present invention as the supernatants disclosed in the present invention contain proteins secreted by *E. coli*. *E. coli* does not secrete intimin. Therefore Dean-Nystrom actually teaches away from such a combination as presently claimed. As discussed above, central to the present invention is cell culture supernatants derived from EHEC cultures which contain EHEC secreted antigens, produce an immune response in animals to which they are administered and thereby provide protection against EHEC infection, such as protection against colonization.

In addition, Dean-Nystrom *et al.* merely states in the abstract and closing paragraph of their paper that “these results *suggest* that experiments to determine *if* intimin-based vaccines reduce O157:H7 levels in cattle are warranted.” (emphasis added by applicants; see abstract). Dean-Nystrom uses new born calves which are susceptible to O157:H7 infection. Older cows do NOT get the disease, but instead just carry and secrete the *E. coli*. Even assuming that the requisite motivation to combine the selected elements of the cited references exists, which applicants deny, the ordinarily skilled artisan would have no reasonable expectation of success in arriving at the presently claimed invention. At best, the examiner’s reasoning amounts only to an obviousness to try rationale; “obvious to try,” however, is not the proper legal standard under 35 U.S.C. § 103. *In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

Furthermore, applicants submit that it is impermissible for the examiner to use the claimed invention as an instruction manual or “template” to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, 972 F.2d 1260, 23 USPQ.2d 1780 (Fed. Cir. 1992). The examiner cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ.2d 1596, 1600 (Fed. Cir. 1988). Applicants submit

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that the examiner is engaging in the impermissible hindsight construction of the applicants' claimed invention.

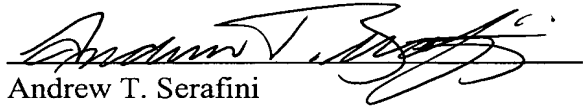
Applicants further submit that the examiner has not established that there would be a reasonable expectation of success of using the *E. coli* disclosed in Dean-Nystrom *et al.* (and the integral membrane protein intimin) with the method disclosed in Allan *et al.* as applied to the claimed invention.

Thus, applicants respectfully submit that a *prima facie* case of obviousness has not been set forth. In view of the foregoing, applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

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